A STUDY OF
100 CASES OF HIV

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CERTIFICATE

This is to certify that the Dissertation entitled ***"A STUDY OF 100 CASES OF HIV"*** *herewith submitted by* ***Dr.P.SANBAKASREE,*** *Post Graduate in General Medicine, Coimbatore Medical College to the Tamilnadu Dr. M.G.R. Medical University, is a record of a bonafide research work carried out by her under my guidance and supervision from January 2006 to June 2007.*

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DECLARATION

*I solemnly declare that the Dissertation titled "**A STUDY OF 100 CASES OF HIV",** was done by me at Coimbatore Medical College & Hospital during the period from January 2006 to June 2007 under the guidance and supervision of **Prof.Dr.M.Ramasamy.M.D.** and **Prof.Dr.S.Veerakesari.M.D.***

This dissertation is submitted to the Tamilnadu Dr. M.G.R. Medical University towards the partial fulfillment of the requirement for the award of M.D. Degree (Branch I) in General Medicine.

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INTRODUCTION

Human immunodeficiency virus (**HIV**) infection in humans is now pandemic. As of January 2006, the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) estimate that AIDS has killed more than 25 million people since it was first recognized on December 1, 1981, making it one of the most destructive pandemics in recorded history. In 2005 alone, between 3.4 and 6.2 million people were newly infected and between 2.4 and 3.3 million people with AIDS died, an increase from 2004 and the highest number since 1981. Globally, between 33.4 and 46 million people currently live with HIV. [1]

Two-thirds of HIV/AIDS infections in Asia occur in India, with an estimated 5.7 million infections (estimated 3.4–9.4 million) (0.9% of population, it accounts for 10% of global HIV burden), surpassing South Africa's estimated 5.5 million (4.9–6.1 million) (11.9% of population) infections, making India the country with the highest number of HIV infections in the world. [2]

HIV/AIDS is no longer just a public health issue in India but become one of the most serious socioeconomic and developmental

concerns because nearly 89% of reported cases are occurring in sexually active and economically productive group of 15 to 44 years.[3]

Although HIV/AIDS is still largely concentrated in at risk populations, data suggests that epidemic is moving beyond these groups in some regions and in general population through the bridging population. [4] It is also moving from urban to rural areas.[5] The spread of HIV in India has been diverse with much of having a low rate of infection and the epidemic being the most extreme in the southern half of the country and in the far north-east. The highest HIV prevalence rates are found in Maharastra, Andhra Pradesh, Karnataka, Manipur and Nagaland. As of July 2005, all of the nationally reported AIDS cases were in Maharastra, Gujarat, Tamilnadu, Andhra Pradesh, Manipur, West Bengal. In the southern states, infections are mostly due to heterosexual contact while infections are mainly found among injecting drug users in Manipur and Nagaland.

HIV infects cells in the immune system and the central nervous system. The main type of cell that HIV infects is the T helper lymphocyte. These cells play a crucial role in the immune system, by coordinating the actions of other immune system cells. A large

reduction in the number of T helper cells seriously weakens the immune system.

HIV infects the T helper cell because it has the protein CD4 on its surface, which HIV uses to attach itself to the cell before gaining entry. This is why the T helper cell is sometimes referred to as a CD4+ lymphocyte. Once it has found its way into a cell, HIV produces new copies of itself, which can then go on to infect other cells.

Over time, HIV infection leads to a severe reduction in the number of T helper cells available to help fight disease. The process usually takes several years.

Following infection with HIV, the rate of clinical disease progression varies enormously between individuals. Many factors such as host susceptibility and immune function, [6][7][8] health care and co-infections, [9]10][11] as well as factors relating to the viral strain [12][13] may affect the rate of clinical disease progression. Symptomatic HIV infection is mainly caused by the emergence of opportunistic infections and cancers that the immune system would normally prevent. These can occur in almost all the body systems.

HIV infection leads to AIDS and major cause of morbidity and mortality of such patients are opportunistic infections. [14]

Epidemiology and clinical features differ from country to country. The clinical features and opportunistic infections may depend on the organisms and the parasites endemic in that country. The diagnosed HIV/AIDS cases represent only tip of the iceberg. High index of suspicion is necessary for the diagnosis. Hence the present study was carried out to elucidate the epidemiological and clinical spectrum of HIV disease, among the HIV seropositive patients admitted in Coimbatore medical college hospital, Coimbatore.

1. To find out common clinical manifestations and various complications of HIV disease.
2. To determine the frequency of occurrence of opportunistic infections in adult HIV/AIDS patients.
3. To find new clinical manifestations of HIV disease, if any.

Human immunodeficiency virus (**HIV**) is a retrovirus that can lead to *acquired immunodeficiency syndrome* (AIDS, a condition in humans in which the immune system begins to fail, leading to life-threatening opportunistic infections). Previous names for the virus include **human T-lymphotropic virus-III** (**HTLV-III**), **lymphadenopathy-associated virus** (**LAV**), or **AIDS-associated retrovirus** (**ARV**).[15][16]

HIV primarily infects vital cells in the human immune system such as helper T cells (specifically $CD4^+$ T cells), macrophages and dendritic cells.

HIV infection leads to low levels of $CD4^+$ T cells through three main mechanisms: firstly, direct viral killing of infected cells; secondly, increased rates of apoptosis in infected cells; and thirdly, killing of infected $CD4^+$ T cells by CD8 cytotoxic lymphocytes that recognize infected cells.

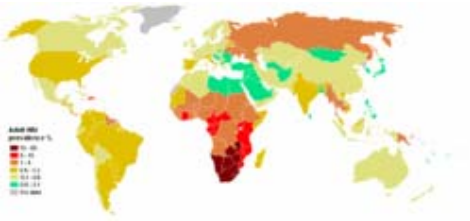
When $CD4^+$ T cell numbers decline below a critical level, cell-mediated immunity is lost, and the body becomes progressively more susceptible to opportunistic infections. If untreated, eventually most HIV-infected individuals develop AIDS (Acquired Immunodeficiency

Syndrome) and die; however about one in ten remains healthy for many years, with no noticeable symptoms. [17]

Treatment with anti-retrovirals, where available, increases the life expectancy of people infected with HIV. It is hoped that current and future treatments may allow HIV-infected individuals to achieve a life expectancy approaching that of the general public.

Epidemiology

AIDS pandemic



Prevalence of HIV among adults per country at the end of 2005 15–50% 5–15% 1–5% 0.5–1.0% 0.1–0.5% <0.1% no data

UNAIDS and the WHO estimate that AIDS has killed more than 25 million people since it was first recognized in 1981, making it one of the most destructive pandemics in recorded history.Despite recent improved access to antiretroviral treatment and care in many regions of the world, the AIDS pandemic claimed an estimated,

2.8 million (between 2.4 and 3.3 million) lives in 2005 of which more than half a million (570,000) were children.[1]

Globally, between 33.4 and 46 million people currently live with HIV.[1] In 2005, between 3.4 and 6.2 million people were newly infected and between 2.4 and 3.3 million people with AIDS died, an increase from 2004 and the highest number since 1981.

Classification

HIV was classified as a member of the genus Lentivirus,[18] part of the family of Retroviridae.[19]

Lentiviruses have many common morphologies and biological properties. Many species are infected by lentiviruses, which are characteristically responsible for long-duration illnesses with a long incubation period.[20]

Lentiviruses are transmitted as single-stranded, positive-sense, enveloped RNA viruses. Upon entry of the target cell, the viral RNA genome is converted to double-stranded DNA by a virally encoded reverse transcriptase that is present in the virus particle. This viral DNA is then integrated into the cellular DNA by a virally encoded integrase so that the genome can be transcribed.

Once the virus has infected the cell, two pathways are possible: either the virus becomes latent and the infected cell continues to function, or the virus becomes active and replicates, and a large number of virus particles are liberated that can then infect other cells.

Transmission

Estimated per act risk for acquisition of HIV-1 by exposure route[24]

Exposure Route	**Estimated infections per 10,000 exposures to an infected source**
Blood Transfusion	9,000[25]
Childbirth	2,500[26]
Needle-sharing injection drug use	67[27]
Receptive anal intercourse*	50[28][29]
Percutaneous needle stick	30[30]
Receptive penile-vaginal intercourse*	10[28][29][31]
Insertive anal intercourse*	6.5[28][29]
Insertive penile-vaginal intercourse*	5[28][29]
Receptive fellatio*	1[29]
Insertive fellatio*	0.5[29]

* assuming no condom use

Since the beginning of the pandemic, three main transmission routes for HIV have been identified:

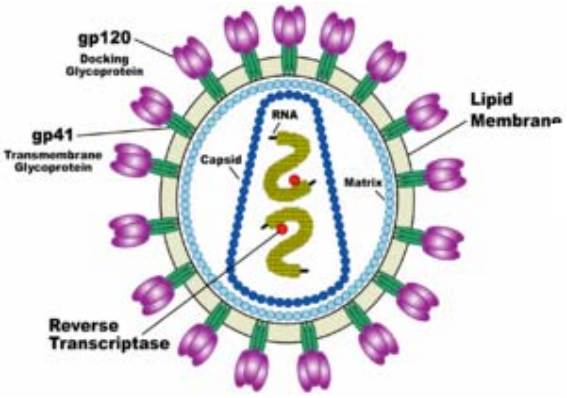
Sexual route. The majority of HIV infections are acquired through unprotected sexual relations. Sexual transmission can occur when infected sexual secretions of one partner come into contact with the genital, oral, or rectal mucous membranes of another.

- **Blood or blood product route.** This transmission route can account for infections in intravenous drug users, hemophiliacs and recipients of blood transfusions (though most transfusions are checked for HIV in the developed world) and blood products. Health care workers such as nurses, laboratory workers, and doctors, have also been infected, although this occurs more rarely. People who give and receive tattoos, piercings, and scarification procedures can also be at risk of infection.
- **Mother-to-child transmission** (MTCT). The transmission of the virus from the mother to the child can occur *in utero* during the last weeks of pregnancy and at childbirth. In the absence of treatment, the transmission rate between the mother and child is 25%.[26] However, where drug treatment and Cesarian section

are available, this can be reduced to 1%.[26] Breast feeding also presents a risk of infection for the baby.

HIV-2 is transmitted much less frequently by the MTCT and sexual route than HIV-1. HIV has been found at low concentrations in the saliva, tears and urine of infected individuals, but there are no recorded cases of infection by these secretions and the potential risk of transmission is negligible.[32] The use of physical barriers such as the latex condom is widely advocated to reduce the sexual transmission of HIV. Spermicide, when used alone or with vaginal contraceptives like a diaphragm, actually increases the male to female transmission rate due to inflammation of the vagina; it should not be considered a barrier to infection.[33]

Structure and genome



It is about 120 nm in diameter (around 60 times smaller than a red blood cell) and roughly spherical.[34]

It is composed of two copies of positive single-stranded RNA that codes for the virus's nine genes enclosed by a conical capsid composed of 2,000 copies of the viral protein p24.[35]

The single-stranded RNA is tightly bound to nucleocapsid proteins, p7 and enzymes needed for the development of the virion such as reverse transcriptase, proteases, ribonuclease and integrase. A matrix composed of the viral protein p17 surrounds the capsid ensuring the integrity of the virion particle.[36] This is, in turn, surrounded by the viral envelope which is composed of two layers of fatty molecules called phospholipids taken from the membrane of a human cell when a newly formed virus particle buds from the cell. Embedded in the viral envelope are proteins from the host cell and about 70 copies of a complex HIV protein that protrudes through the surface of the virus particle.[35] This protein, known as Env, consists of a cap made of three molecules called glycoprotein (gp) 120, and a stem consisting of three gp41 molecules that anchor the structure into the viral envelope.[36] This glycoprotein complex enables the virus to attach to and fuse with target cells to initiate the infectious cycle.[36] Both these surface proteins, especially gp120, have been considered as targets of future treatments or vaccines against HIV.[37] Of the nine genes that are encoded within the RNA genome, three of these genes,

gag, *pol*, and *env*, contain information needed to make the structural proteins for new virus particles.[35] *env*, for example, codes for a protein called gp160 that is broken down by a viral enzyme to form gp120 and gp41. The six remaining genes, *tat*, *rev*, *nef*, *vif*, *vpr*, and *vpu* (or *vpx* in the case of HIV-2), are regulatory genes for proteins that control the ability of HIV to infect cells, produce new copies of virus (replicate), or cause disease. [35] The protein encoded by *nef*, for instance, appears necessary for the virus to replicate efficiently, and the *vpu*-encoded protein influences the release of new virus particles from infected cells.[35] The ends of each strand of HIV RNA contain an RNA sequence called the long terminal repeat (LTR). Regions in the LTR act as switches to control production of new viruses and can be triggered by proteins from either HIV or the host cell. [35]

Tropism

The term *viral tropism* refers to which cell types HIV infects. HIV can infect a variety of immune cells such as $CD4^+$ T cells, macrophages, and microglial cells. HIV-1 entry to macrophages and $CD4^+$ T cells is mediated through interaction of the virion envelope glycoproteins (gp120) with the CD4 molecule on the target cells and also with chemokine coreceptors.[36]

Macrophage (M-tropic) strains of HIV-1, or non-syncitia-inducing strains (NSI) use the β-chemokine receptor CCR5 for entry and are thus able to replicate in macrophages and $CD4^+$ T cells.[38] Indeed, macrophages play a key role in several critical aspects of HIV infection. They appear to be the first cells infected by HIV and perhaps the source of HIV production when $CD4^+$ cells become depleted in the patient. Macrophages and microglial cells are the cells infected by HIV in the central nervous system. In tonsils and adenoids of HIV-infected patients, macrophages fuse into multinucleated giant cells that produce huge amounts of virus

T-tropic isolates, or syncitia-inducing (SI) strains replicate in primary $CD4^+$ T cells as well as in macrophages and use the α-chemokine receptor, CXCR4, for entry.[38][39][40]

The α-chemokine, SDF-1, a ligand for CXCR4, suppresses replication of T-tropic HIV-1 isolates. It does this by down-regulating the expression of CXCR4 on the surface of these cells. HIV that use only the CCR5 receptor are termed R5, those that only use CXCR4 are termed X4, and those that use both, X4R5. However, the use of coreceptor alone does not explain viral tropism, as not all R5 viruses are able to use CCR5 on macrophages for a productive infection[38]

HIV can also infect a subtype of myeloid dendritic cells,[41] which probably constitute a reservoir that maintains infection when $CD4^+$ T cell numbers have declined to extremely low levels.

Sexual intercourse is the major mode of HIV transmission. Both X4 and R5 HIV are present in the seminal fluid which is passed from partner to partner.

In patients infected with subtype B HIV-1, there is often a co-receptor switch in late-stage disease and T-tropic variants appear that can infect a variety of T cells through CXCR4.[42] These variants then replicate more aggressively with heightened virulence that causes rapid T cell depletion, immune system collapse, and opportunistic infections that mark the advent of AIDS.[43] Thus, during the course of infection, viral adaptation to the use of CXCR4 instead of CCR5 may be a key step in the progression to AIDS.

A number of studies with subtype B-infected individuals have determined that between 40 and 50% of AIDS patients can harbour viruses of the SI, and presumably the X4, phenotype.[44][45]

The HIV replication cycle

Entry into the cell

HIV enters macrophages and $CD4^+$ T cells by the adsorption of glycoproteins on its surface to receptors on the target cell followed by fusion of the viral envelope with the cell membrane and the release of the HIV capsid into the cell.[46][47]

Once HIV has bound to the target cell, the HIV RNA and various enzymes, including reverse transcriptase, integrase, ribonuclease and protease, are injected into the cell.[46]

HIV can infect dendritic cells (DCs) by this CD4-CCR5 route, but another route using mannose-specific C-type lectin receptors such as DC-SIGN can also be used.[48] DCs are one of the first cells encountered by the virus during sexual transmission. They are currently thought to play an important role by transmitting HIV to T cells once the virus has been captured in the mucosa by DCs.[48]

Replication and transcription

Once the viral capsid enters the cell, an enzyme called *reverse transcriptase* liberates the single-stranded (+)RNA from the attached viral proteins and copies it into a complementary DNA.[49] This process of reverse transcription is extremely error-prone and it is

during this step that mutations may occur. Such mutations may cause drug resistance. The reverse transcriptase then makes a complementary DNA strand to form a double-stranded viral DNA intermediate (vDNA). This vDNA is then transported into the cell nucleus. The integration of the viral DNA into the host cell's genome is carried out by another viral enzyme called *integrase*.

This integrated viral DNA may then lie dormant, in the latent stage of HIV infection. [49] To actively produce the virus, certain cellular transcription factors need to be present, the most important of which is NF-κB (NF kappa B), which is upregulated when T cells become activated.[50] This means that those cells most likely to be killed by HIV are in fact those currently fighting infection.

In this replication process, the integrated provirus is copied to mRNA which is then spliced into smaller pieces. These small pieces produce the regulatory proteins Tat (which encourages new virus production) and Rev. As Rev accumulates it gradually starts to inhibit mRNA splicing.[51] At this stage, the structural proteins Gag and Env are produced from the full-length mRNA. The full-length RNA is actually the virus genome; it binds to the Gag protein and is packaged into new virus particles.

HIV-1 and HIV-2 appear to package their RNA differently; HIV-1 will bind to any appropriate RNA whereas HIV-2 will preferentially bind to the mRNA which was used to create the Gag protein itself. This may mean that HIV-1 is better able to mutate (HIV-1 infection progresses to AIDS faster than HIV-2 infection and is responsible for the majority of global infections).

Assembly and release

The final step of the viral cycle, assembly of new HIV-1 virons, begins at the plasma membrane of the host cell. The Env polyprotein (gp160) goes through the endoplasmic reticulum and is transported to the Golgi complex where it is cleaved by protease and processed into the two HIV envelope glycoproteins gp41 and gp120. These are transported to the plasma membrane of the host cell where gp41 anchors the gp120 to the membrane of the infected cell. The Gag (p55) and Gag-Pol (p160) polyproteins also associate with the inner surface of the plasma membrane along with the HIV genomic RNA as the forming virion begins to bud from the host cell. Maturation either occurs in the forming bud or in the immature virion after it buds from the host cell. During maturation, HIV proteases cleave the polyproteins into individual functional HIV proteins and enzymes. The various structural components then assemble to produce a mature

HIV virion.[52] This cleavage step can be inhibited by protease inhibitors. The mature virus is then able to infect another cell.

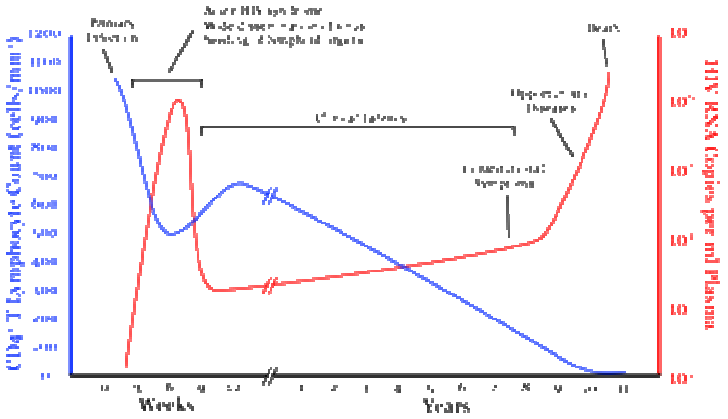
The clinical course of infection

The initial infection with HIV generally occurs after transfer of body fluids from an infected person to an uninfected one.

The first stage of infection, the primary, or acute infection, is a period of rapid viral replication that immediately follows the individual's exposure to HIV leading to an abundance of virus in the peripheral blood with levels of HIV commonly approaching several million viruses per mL.[53] This response is accompanied by a marked drop in the numbers of circulating $CD4^+$ T cells. This acute viremia is associated in virtually all patients with the activation of $CD8^+$ T cells, which kill HIV-infected cells, and subsequently with antibody production, or seroconversion.

The $CD8^+$ T cell response is thought to be important in controlling virus levels, which peak and then decline, as the $CD4^+$ T cell counts rebound to around 800 cells per mL (the normal value is 1200 cells per mL). A good $CD8^+$ T cell response has been linked to slower disease progression and a better prognosis, though it does not eliminate the virus.[54]

During this period (usually 2-4 weeks post-exposure) most individuals (80 to 90%) develop an influenza or mononucleosis-like illness called acute HIV infection, the most common symptoms of which may include fever, lymphadenopathy, pharyngitis, rash, myalgia, malaise, mouth and esophagal sores, and may also include, but less commonly, headache, nausea and vomiting, enlarged liver/spleen, weight loss, thrush, and neurological symptoms. Infected individuals may experience all, some, or none of these symptoms. Symptoms have an average duration of 28 days and usually last at least a week although duration of symptoms may vary.[55] Because of the nonspecific nature of these illnesses, it is often not recognized as a sign of HIV infection. Even if patients go to their doctors or a hospital, they will often be misdiagnosed as having one of the more common infectious diseases with the same symptoms. Consequently, these primary symptoms are not used to diagnose HIV infection as they do not develop in all cases and because many are caused by other more common diseases. However, recognizing the syndrome can be important because the patient is much more infectious during this period.



A generalized graph of the relationship between HIV copies (viral load) and CD4 counts over the average course of untreated HIV infection; any particular individual's disease course may vary considerably. $CD4^+$ T cell count (cells per μL) HIV RNA copies per mL of plasma

A strong immune defense reduces the number of viral particles in the blood stream, marking the start of the infection's clinical latency stage. Clinical latency can vary between two weeks and 20 years. During this early phase of infection, HIV is active within lymphoid organs, where large amounts of virus become trapped in the follicular dendritic cells (FDC) network.[56] The surrounding tissues that are rich in $CD4^+$ T cells may also become infected, and viral particles accumulate both in infected cells and as free virus. Individuals who are in this phase are still infectious. During this time, $CD4^+$ $CD45RO^+$ T cells carry most of the proviral load.[57]

When $CD4^+$ T cell numbers decline below a critical level, cell-mediated immunity is lost, and infections with a variety of opportunistic microbes appear. The first symptoms often include moderate and unexplained weight loss, recurring respiratory tract infections (such as sinusitis, bronchitis, otitis media, pharyngitis), prostatitis, skin rashes, and oral ulcerations. Common opportunistic infections and tumors, most of which are normally controlled by robust $CD4^+$ T cell-mediated immunity then start to affect the patient.

Typically, resistance is lost early on to oral Candida species and to *Mycobacterium tuberculosis*, which leads to an increased susceptibility to oral candidiasis (thrush) and tuberculosis. Later, reactivation of latent herpes viruses may cause worsening recurrences of herpes simplex eruptions, shingles, Epstein-Barr virus-induced B-cell lymphomas, or Kaposi's sarcoma, a tumor of endothelial cells that occurs when HIV proteins such as Tat interact with Human Herpesvirus-8. Pneumonia caused by the fungus *Pneumocystis jirovecii* is common and often fatal. In the final stages of AIDS, infection with cytomegalovirus (another herpes virus) or Mycobacterium avium complex is more prominent. Not all patients with AIDS get all these infections or tumors, and there are other tumors and infections that are less prominent but still significant.

Over time the immune system becomes severely damaged by HIV. This is thought to happen for three main reasons:

- The lymph nodes and tissues become damaged or 'burnt out' because of the years of activity;
- HIV mutates and becomes more pathogenic, in other words stronger and more varied, leading to more T helper cell destruction;
- The body fails to keep up with replacing the T helper cells that are lost.

As the immune system fails, so symptoms develop. Initially many of the symptoms are mild, but as the immune system deteriorates the symptoms worsen.

Sites of opportunistic infections and cancers :

Symptomatic HIV infection is mainly caused by the emergence of opportunistic infections and cancers that the immune system would normally prevent. These can occur in almost all the body systems, but common examples are featured in the table below.

As the table below indicates, symptomatic HIV infection is often characterised by multi-system disease. Treatment for the specific

infection or cancer is often carried out, but the underlying cause is the action of HIV as it erodes the immune system. Unless HIV itself can be slowed down the symptoms of immune suppression will continue to worsen.

System	Examples of Infection/Cancer
Respiratory system	• Tuberculosis (TB) • Pneumocystis carinii Pneumonia (PCP) • Kaposi's Sarcoma (KS)
Gastro-intestinal system	• Candida • Cryptosporidiosis • Cytomegalovirus (CMV) • Isosporiasis • Kaposi's Sarcoma • Giardiasis
Central/peripheral Nervous system	• HIV encephalopathy • Cryptococcosis • Varicella Zoster • Herpes simplex • Cytomegalovirus • Toxoplasmosis • Non Hodgkin's lymphoma
Skin	• Herpes simplex • Varicella Zoster • Kaposi's sarcoma

CDC Classification System for HIV Infection[58] [59]

The CDC categorization of HIV/AIDS is based on the lowest documented CD4 cell count (Table 1) and on previously diagnosed HIV-related conditions (Tables 2 and 3). For example, if a patient had

a condition that once met the criteria for Category B but now is asymptomatic, the patient would remain in Category B. Additionally, categorization is based on specific conditions, as indicated below. Patients in categories A3, B3, and C1-C3 are considered to have AIDS.

Table 1. CDC Classification System for HIV-Infected Adults and Adolescents

CD4 Cell Categories	Clinical Categories		
	A Asymptomatic, Acute HIV, or PGL	**B** Symptomatic Conditions,#* not A or C	**C** AIDS-Indicator Conditions*
(1) ≥500 cells/µL	A1	B1	C1
(2) 200-499 cells/µL	A2	B2	C2
(3) <200 cells/µL	A3	B3	C3

Key to abbreviations: CDC = U.S. Centers for Disease Control and Prevention; PGL = persistent generalized lymphadenopathy.

For symptomatic conditions, see Table 2. * For AIDS-indicator conditions, see Table 3.

Table 2. CDC Classification System: Category B Symptomatic Conditions

Category B symptomatic conditions are defined as symptomatic conditions occurring in an HIV-infected adolescent or adult that meet at least 1 of the following criteria:

a) They are attributed to HIV infection or indicate a defect in cell-mediated immunity.

b) They are considered to have a clinical course or management that is complicated by HIV infection.

Examples include, but are not limited to, the following:

Bacillary angiomatosis

Oropharyngeal candidiasis (thrush)

Vulvovaginal candidiasis, persistent or resistant

Pelvic inflammatory disease (PID)

Cervical dysplasia (moderate or severe)/cervical carcinoma in situ

Hairy leukoplakia, oral

Idiopathic thrombocytopenic purpura

Constitutional symptoms, such as fever (>38.5°C) or diarrhea lasting >1 month

Peripheral neuropathy

Herpes zoster (shingles), involving ≥2 episodes or ≥1 dermatome

Table 3. CDC Classification System: Category C AIDS-Indicator Conditions

Bacterial pneumonia, recurrent (≥2 episodes in 12 months)
Candidiasis of the bronchi, trachea, or lungs
Candidiasis, esophageal
Cervical carcinoma, invasive, confirmed by biopsy
Coccidioidomycosis, disseminated or extrapulmonary
Cryptococcosis, extrapulmonary
Cryptosporidiosis, chronic intestinal (>1-month duration)
Cytomegalovirus disease (other than liver, spleen, or nodes)
Encephalopathy, HIV-related
Herpes simplex: chronic ulcers (>1-month duration), or bronchitis, pneumonitis, or esophagitis
Histoplasmosis, disseminated or extrapulmonary
Isosporiasis, chronic intestinal (>1-month duration)
Kaposi sarcoma
Lymphoma, Burkitt, immunoblastic, or primary central nervous system
Mycobacterium avium complex (MAC) or *M kansasii*, disseminated or extrapulmonary
Mycobacterium tuberculosis, pulmonary or extrapulmonary
Mycobacterium, other species or unidentified species, disseminated or extrapulmonary
Pneumocystis jiroveci (formerly *carinii*) pneumonia (PCP)
Progressive multifocal leukoencephalopathy (PML)
Salmonella septicemia, recurrent (nontyphoid)
Toxoplasmosis of brain
Wasting syndrome due to HIV (involuntary weight loss >10% of baseline body weight) associated with either chronic diarrhea (≥2 loose stools per day ≥1 month) or chronic weakness and documented fever ≥1 month

WHO clinical staging of HIV disease in adults and adolescents (2006 revision) [58] [59]

Staging is based on clinical findings that guide the diagnosis, evaluation, and management of HIV/AIDS, and does not require a CD4 cell count. This staging system is used in many countries to determine eligibility for antiretroviral therapy. Clinical stages are categorized as 1 through 4, progressing from primary HIV infection to advanced HIV/AIDS. These stages are defined by specific clinical conditions or symptoms. For the purpose of the WHO staging system, adolescents and adults are defined as individuals aged ≥15 years.

WHO Clinical Staging of HIV/AIDS for Adults and Adolescents (Interim Definitions)

Primary HIV Infection

Asymptomatic

Acute retroviral syndrome

Clinical Stage 1

Asymptomatic

Persistent generalized lymphadenopathy

Clinical Stage 2

Moderate unexplained weight loss (<10% of presumed or measured body weight)

Recurrent respiratory infections (respiratory tract infections, upper respiratory infections, sinusitis, bronchitis, otitis media, pharyngitis)

Herpes zoster

Minor mucocutaneous manifestations (angular cheilitis, recurrent oral ulcerations, seborrheic dermatitis, prurigo, papular pruritic eruptions, fungal fingernail infections)

Clinical Stage 3

Conditions for which a presumptive diagnosis can be made on the basis of clinical signs or simple investigations

Severe weight loss (>10% of presumed or measured body weight)

Unexplained chronic diarrhea for >1 month

Unexplained persistent fever for >1 month (intermittent or constant)

Oral candidiasis (thrush)

Oral hairy leukoplakia

Pulmonary tuberculosis within the last 2 years

Severe presumed bacterial infections (eg, pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteremia)

Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis

Conditions for which confirmatory diagnostic testing is necessary

Unexplained anemia (hemoglobin <8 g/dL)

Neutropenia (neutrophils <500 cells/µL)

Thrombocytopenia (platelets <50,000 cells/µL)

Clinical Stage 4

Conditions for which a presumptive diagnosis can be made on the basis of clinical signs or simple investigations

HIV wasting syndrome, as defined by the CDC (see Table 3, above)

Pneumocystis jiroveci (formerly *carinii*) pneumonia

Recurrent severe or radiologic bacterial pneumonia

Chronic herpes simplex infection (oral or genital, or anorectal site) for >1 month

Esophageal candidiasis

Extrapulmonary tuberculosis

Kaposi sarcoma

Central nervous system toxoplasmosis

HIV encephalopathy

Conditions for which a confirmatory diagnostic testing is necessary

Cryptococcosis, extrapulmonary

Disseminated nontuberculosis *Mycobacteria* infection

Progressive multifocal leukoencephalopathy

Candida of the trachea, bronchi, or lungs

Cryptosporidiosis

Isosporiasis

Visceral herpes simplex infection, cytomegalovirus infection (retinitis or organ other than liver, spleen, or lymph node)

Any disseminated mycosis (eg, histoplasmosis, coccidioidomycosis, penicilliosis)

Recurrent nontyphoidal Salmonella septicemia

Lymphoma (cerebral or B-cell non-Hodgkin)

Invasive cervical carcinoma

Visceral leishmaniasis

HIV encephalopathy: clinical findings of disabling cognitive and/or motor dysfunction interfering with activities of daily living, progressing over weeks to months, in the absence of a concurrent illness or condition other than HIV infection which could explain the findings.

HIV test

HIV-1 testing consists of initial screening with an enzyme-linked immunosorbent assay (ELISA) to detect antibodies to HIV-1.

Confirmatory testing with a more specific supplemental test (e.g., Western blot or, less commonly, an immunofluorescence assay (IFA))

Generally, a second specimen should be collected more than a month later and retested for persons with indeterminate Western blot results

Nucleic acid testing (e.g., viral RNA or proviral DNA amplification method) can also help diagnosis in certain situations.[60]

In addition, a few tested specimens might provide inconclusive results because of a low quantity specimen. In these situations, a second specimen is collected and tested for HIV infection.

Treatment

There is currently no vaccine or cure for HIV or AIDS. The only known method of prevention is avoiding exposure to the virus. However, an antiretroviral treatment, known as post-exposure prophylaxis is believed to reduce the risk of infection if begun directly after exposure.[61] Current treatment for HIV infection consists of highly active antiretroviral therapy, or HAART.[62]

Classes of antiretroviral drugs

Antiretroviral drugs are broadly classified by the phase of the retrovirus life-cycle that the drug inhibits. There are thus six broad classifications of antiretroviral drugs in development, though only the first three classes currently have licensed examples:

- Reverse transcriptase inhibitors (RTIs) target construction of viral DNA by inhibiting activity of reverse transcriptase. There are two subtypes of RTIs with different mechanisms of action: nucleoside-analogue RTIs are incorporated into the viral DNA leading to chain termination, while non-nucleoside-analogue RTIs distort the binding potential of the reverse transcriptase enzyme.
- Protease inhibitors (PIs) target viral assembly by inhibiting the activity of protease, an enzyme used by HIV to cleave nascent proteins for final assembly of new virons.
- Fusion inhibitors block HIV from fusing with a cell's membrane to enter and infect it. There is currently only one FDA-approved drug in this class, enfuvirtide,
- Integrase inhibitors inhibit the enzyme integrase, which is responsible for integration of viral DNA into the DNA of the infected cell. There are several integrase inhibitors currently

under clinical trial, and raltegravir became the first to receive FDA approval in October 2007.

- Entry inhibitors block HIV-1 from the host cell by binding CCR5, a molecule on the host membrane termed a co-receptor that HIV-1 normally uses for entry into the cell together with a primary receptor. Only one entry-inhibitor class drug is available, maraviroc.
- Maturation inhibitors inhibit the last step in gag processing in which the viral capsid polyprotein is cleaved, thereby blocking the conversion of the polyprotein into the mature capsid protein (p24). Because these viral particles have a defective core, the virions released consist mainly of non-infectious particles. Bevirimat is the only drug that is currently under investigation.[63]
- Portmanteau inhibitors A new way to combat HIV through the merging of two antiviral agents into one drug, achieving the same effect as when two or more drugs are taken separately.

Combination therapy

- antiretroviral *combination therapy* defends against resistance by suppressing HIV replication as much as possible.

- Combinations of antiretrovirals create multiple obstacles to HIV replication to keep the number of offspring low and reduce the possibility of a superior mutation. If a mutation arises that conveys resistance to one of the drugs being taken, the other drugs continue to suppress reproduction of that mutation.
- Combinations usually comprise two nucleoside-analogue RTIs and one non-nucleoside-analogue RTI or protease inhibitor.[64] This three drug combination is commonly known as a triple cocktail.[65]
- Combinations of antiretrovirals are subject to positive and negative synergies, which limits the number of useful combinations.
- Other issues further limit some people's treatment options from antiretroviral drug combinations, including their complicated dosing schedules and often severe side effects.

Current treatment guidelines

The current guidelines for antiretroviral therapy (ART) from the World Health Organization reflect the 2003 changes to the guidelines and recommend that in resource-limited settings (that is, developing nations), HIV-infected adults and adolescents should start ART when

HIV infection has been confirmed and one of the following conditions is present [66]):

- Clinically advanced HIV disease;
- WHO Stage IV HIV disease, irrespective of the CD4 cell count;
- WHO Stage III disease with consideration of using CD4 cell counts less than 350/µl to assist decision making;
- WHO Stage I or II HIV disease with CD4 cell counts less than 200/µl.

The current guidelines for adults and adolescents were stated on October 6, 2005 [67]:

- All patients with history of an AIDS-defining illness or severe symptoms of HIV infection regardless of CD4+ T cell count receive ART.
- Antiretroviral therapy is also recommended for asymptomatic patients with less than 200 CD4+ T cells/µl.
- Asymptomatic patients with CD4+ T cell counts of 201–350 cells/µl should be offered treatment.
- For asymptomatic patients with CD4+ T cell of greater than 350 cells/µl and plasma HIV RNA greater than 100,000 copies/ml,

most experienced clinicians defer therapy but some clinicians may consider initiating treatment.

- Therapy should be deferred for patients with CD4+ T cell counts of greater than 350 cells/µl and plasma HIV RNA less than 100,000 copies/mL.

The preferred initial regimens are[68]:

- efavirenz + zidovudine + lamivudine
- efavirenz + tenofovir + emtricitabine
- lopinavir boosted with ritonavir + zidovudine + lamivudine
- lopinavir boosted with ritonavir + tenofovir + emtricitabine.

Postexposure Prophylaxis [PEP]

In 2005, the Centers for Disease Control and Prevention in the United States recommended a 28-day HIV drug regimen for those who have been exposed to HIV (HIV Postexposure Prophylaxis [PEP])[69]. The drugs have demonstrated effectiveness in preventing the virus nearly 100% of the time in those who received treatment within the initial 24 hours of exposure. The effectiveness falls to 52% of the time in those who

are treated within 72 hours; those not treated within the first 72 hours are not recommended candidates for the regimen.

Adverse effects

Adverse effects of antiretroviral drugs vary by drug, by ethnicity, and by individual, and by interaction with other drugs, including alcohol. Hypersensitivity to some drugs may also occur in some individuals. The following list is not complete, but includes several of the common adverse effects experienced by patients taking some antiretroviral drugs:

- Abdominal pain , Alopecia, Anemia, Asthenia
- Change in taste perception
- Diarrhea, Dizziness (Vertigo)
- Fanconi syndrome , Flatulence
- Headache, Hepatitis, Hyperbilirubinemia, Hypercholesterolemia (Dyslipidemia, Hyperlipidemia, high cholesterol)
- Hyperpigmentation (of nails, palms, or soles)
- Ingrown nails, Insomnia
- Jaundice
- Lipodystrophy, Liver failure
- Malaise, confusion, Myalgia

- Myalgic Encephalomyelitis (chronic fatigue syndrome),
- Myopathy
- Nausea, Neutropenia, Nightmares
- Oral ulcers
- Pancreatitis , Paresthesia (numbness), Peripheral neuropathy
- Rash, Renal failure or insufficiency
- Somnolence (drowsiness), Stevens-Johnson syndrome
- Vomiting
- Xeroderma (dry skin)

HAART allows the stabilisation of the patient's symptoms and viremia, but it neither cures the patient, nor alleviates the symptoms, and high levels of HIV-1, often HAART resistant, return once treatment is stopped. Moreover, it would take more than a lifetime for HIV infection to be cleared using HAART. Despite this, many HIV-infected individuals have experienced remarkable improvements in their general health and quality of life, which has led to a large reduction in HIV-associated morbidity and mortality in the developed world. A computer based study in 2006 projected that following the 2004 United States treatment guidelines gave an average life expectancy of an HIV infected individual to be 32.1 years from the time of infection if treatment was started when the CD4 count was

350/μL. This study was limited as it did not take into account possible future treatments and the projection has not been confirmed within a clinical cohort setting. In the absence of HAART, progression from HIV infection to AIDS has been observed to occur at a median of between nine to ten years and the median survival time after developing AIDS is only 9.2 months. However, HAART sometimes achieves far less than optimal results, in some circumstances being effective in less than fifty percent of patients. This is due to a variety of reasons such as medication intolerance/side effects, prior ineffective antiretroviral therapy and infection with a drug-resistant strain of HIV. However, non-adherence and non-persistence with antiretroviral therapy is the major reason most individuals fail to benefit from HAART. The reasons for non-adherence and non-persistence with HAART are varied and overlapping. Major psychosocial issues, such as poor access to medical care, inadequate social supports, psychiatric disease and drug abuse contribute to non-adherence. The complexity of these HAART regimens, whether due to pill number, dosing frequency, meal restrictions or other issues along with side effects that create intentional non-adherence also contribute to this problem. The side effects include lipodystrophy, dyslipidaemia, insulin resistance, an increase in cardiovascular risks and birth defects.

MATERIAL AND METHODS

MATERIAL AND METHODS

The present study was conducted at Coimbatore medical college hospital, Coimbatore. Descriptive study of HIV positive in-patient of Department of Medicine, Coimbatore medical college hospital, Coimbatore. All patients were HIV test positive as determined by ELISA method, using two different antigens and a rapid test as recommended by National AIDS Control Organization (NACO). A total of 100 HIV seropositive patients admitted in Coimbatore medical college hospital, Coimbatore, during January 2006 to June 2007 were investigated for various opportunistic pathogens. Patients on Highly Active Anti-Retro Viral Therapy were not included in the study. A written informed consent was taken from all the patients. The information on each patient's occupation, education, medical history and physical examination was recorded. Laboratory results and clinical findings were used for making the definitive or presumptive diagnosis of each infection.

Basic investigations like urine complete examination, complete haemogram, blood sugar, urea, serum creatinine, electrolytes, liver function tests, ECG, X-ray chest, ultrasonogram abdomen were done. Pleural fluid analysis, cerebrospinal fluids (CSF) analysis, computed tomography were done in relevant cases.

Various samples e.g.: sputum, blood, stool, urine, cerebrospinal fluids (CSF), lymph node aspirate were collected as per symptoms and clinical presentations under universal aseptic precautions in suitable sterile containers. Specimens were stained using appropriate stains e.g. Gram, Giemsa, Ziehl - Neelson and examined under microscope. CSF samples were examined for Cryptococcus by Indian ink wet mount. Appropriate media like Blood agar, MacConkey agar, Chocolate agar and Sabourauds Dextrose agar were used for isolation of pathogens. The pathogens isolated were further identified following standard protocol.

The sera were examined for Syphilis (VDRL test), Hepatitis B (HbsAg), Typhoid (Widal test). Statistical analysis was done using proportions.

OBSERVATION AND RESULTS

OBSERVATIONS

TABLE – 1

AGE AND SEX DISTRIBUTION

Age	Male [n=80]		Female [n=20]		TOTAL [n=100]	
	No.	%	No.	%	No.	%
10 – 19	1	1.25%	1	5%	2	2%
20 – 29	8	10%	4	20%	12	12%
30 – 39	43	53.75%	9	45%	52	52%
40 – 49	22	27.5%	4	20%	26	26%
50 – 60	6	7.5%	2	10%	8	8%
15-44	65	81.25%	17	85%	82	82%

A total of 100 HIV seropositive patients were included in the study group. The age and sex distribution of the cases is shown in the [Table - 1]. 20% were females and 80% were males. The most common age group infected had age in the range of 30-39 years, followed by 40-49 years and 20-29 years.

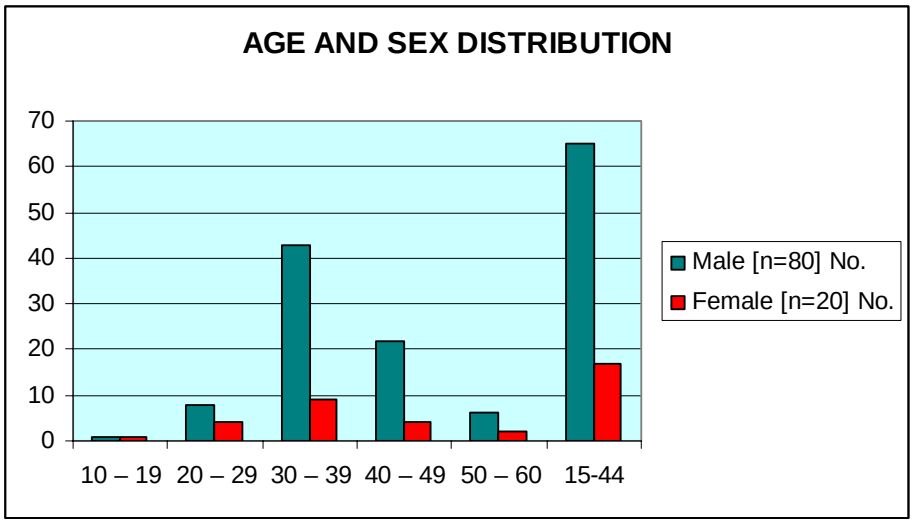


TABLE – 2

MARITAL STATUS - SEX WISE ANALYSIS

Marital Status	Male [n=80]		Female [n=20]		TOTAL [n=100]	
	No.	%	No.	%	No.	%
Married	59	73.75%	13	65%	73	73%
Unmarried	16	20%	_	_	16	16%
Separated	6	7.5%	2	10%	7	7%
Widow	_	_	5	25%	5	5%

Marital Status of the cases is shown in the [Table - 2]. Majority of the male patients were married (73.75%), 20% were not married and 7.5% were separated. All female patients in the study group were married and 25% were widow.

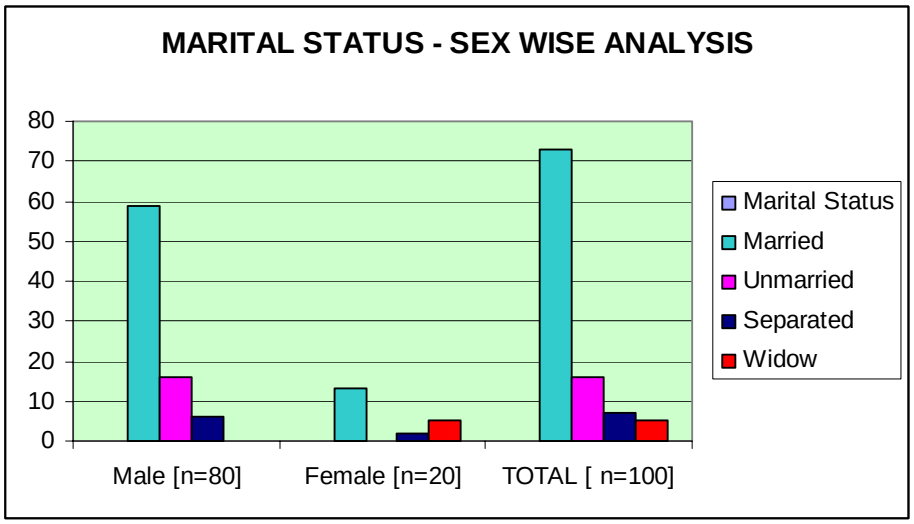


TABLE – 3

OCCUPATON - SEX WISE ANALYSIS

Occupation	Male [n=80]		Female [n=20]		TOTAL [n=100]	
	No.	%	No.	%	No	%.
Labourer	32	40%	4	20%	36	36%
Driver	17	21.25%	-	-	17	17%
Business	11	13.75%	-	-	12	12%
Agriculture	5	6.25%	2	10%	7	7%
At Home	2	2.5%	13	65%	15	15%
Others	13	16.25%	1	5%	13	13%

Others - Painter, Cook, Electrician, Handcraft, Iron casting, Videographer, Gold smith.

Occupation of the cases is shown in the [Table - 3]. It was seen that 21.5% of the affected males were drivers and 40% were labourers. Most of the [65%] affected females were housewives and 20% were labourers.

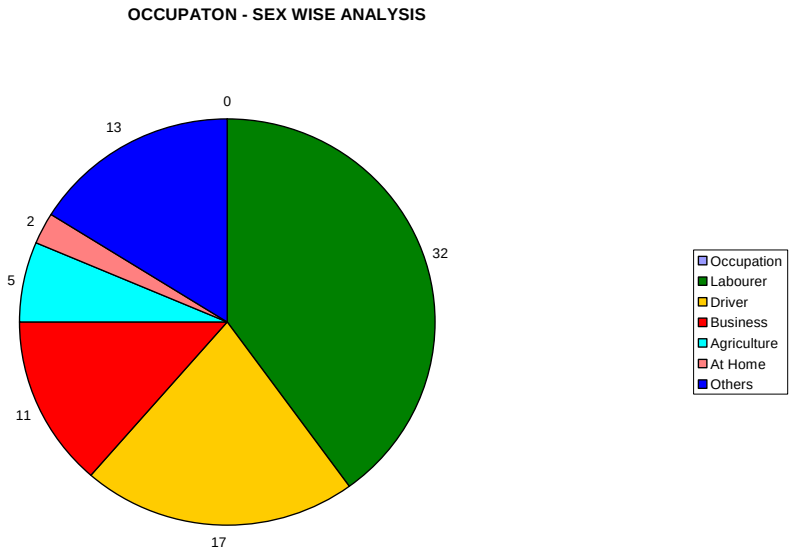


TABLE – 4
LITERACY STATUS - SEX WISE ANALYSIS

Education	Male [n=80]		Female [n=20]		TOTAL[n=100]	
	No.	%	No.	%	No.	%
Illiterate	29	36.25%	10	50%	39	39%
Primary Education	15	18.75%	7	35%	22	22%
Secondary Education up to 8th std	20	25%	2	10%	22	22%
Higher secondary	16	20%	1	5%	17	17%

Literacy status of the cases is shown in the [Table - 4]. Most of the [39%] affected patients were illiterate.

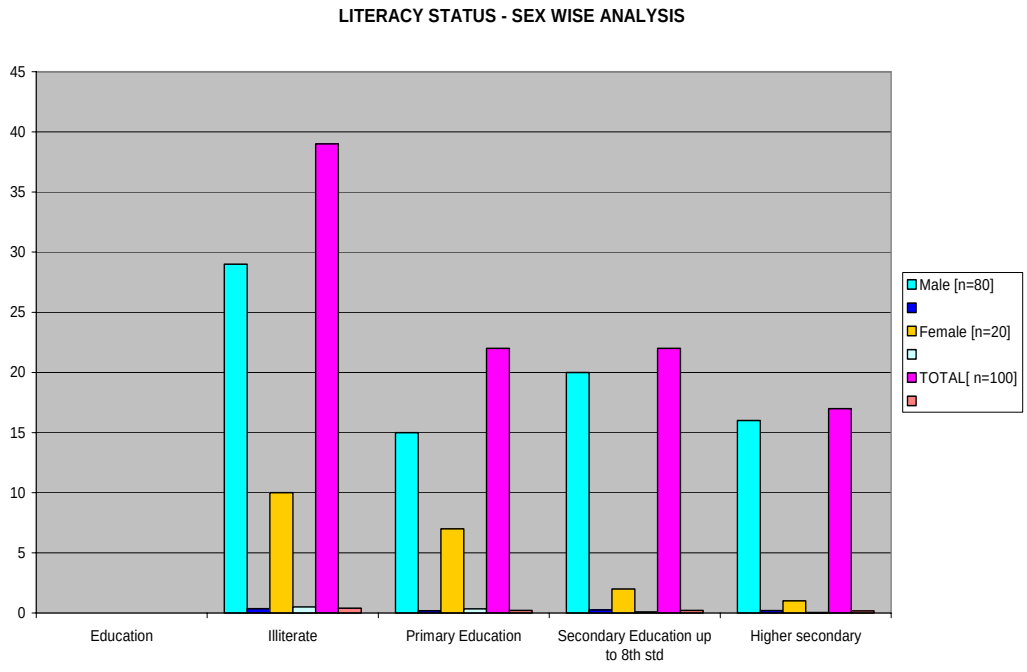


TABLE – 5

DURATION OF POSITIVITY KNOWN TO THE PATIENT

Duration of positivity known	No of cases	%
< 1 Month	30	30%
1to 6 Months	52	52%
6 Months to 1 year	6	6%
>1 year	12	12%

Table -5 shows the duration of positivity known to the patient. 30% of cases came to know about their HIV positivity status only after admission in hospital for their illness. 52% were aware for about 1to 6 months.

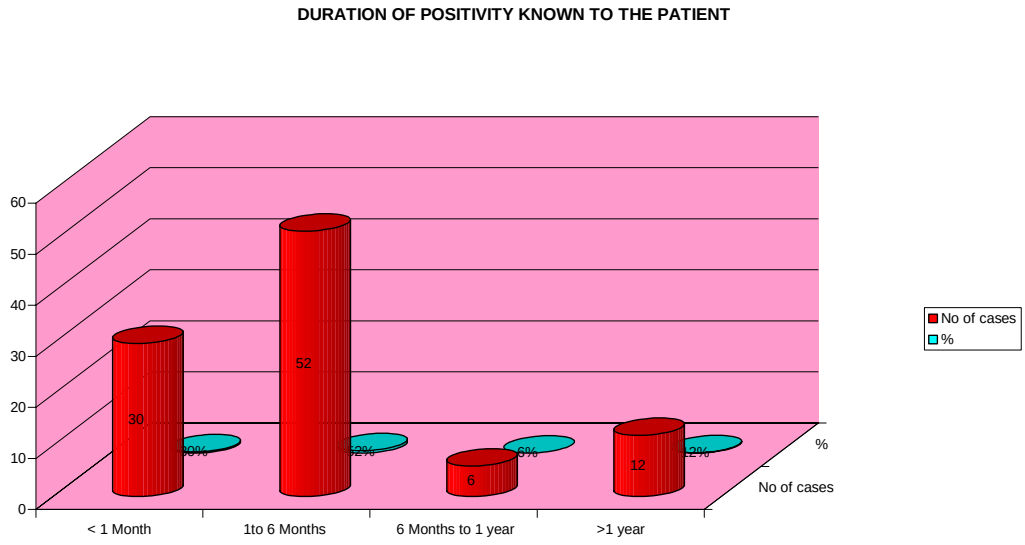


TABLE – 6

MODE OF TRANSMISSION OF HIV

Mode of Transmission	Male [n=80]		Female [n=20]		TOTAL[n=100]	
	No.	%	No.	%	No.	%
Pre marital contact	41	51.25%	_	_	41	41%
Extra marital	46	57.5%	2	10%	48	48%
Marital	-	-	18	90%	18	18%
Vertical transmission	1	1.25%	_	_	1	1%

Mode of transmission of HIV is shown in the [Table - 6]. Most common mode of transmission of HIV infection is sexual. Most of the male patients were married and had history of extramarital contact [57.5%], 51.25% had history of premarital contact and one case acquired through vertical transmission. Among females 90% acquired infection through their husbands and 10% through extra marital contact.

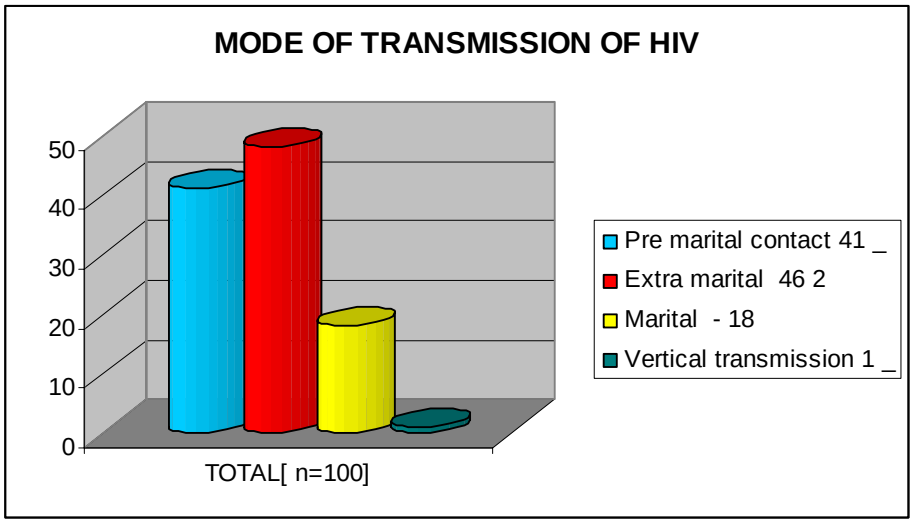


TABLE – 7

ASSOCIATED CLINICAL SYMPTOMS IN HIV POSITIVE PATIENTS

SYMPTOMS	No of cases	< 1 Month		> 1 Month		TOTAL	
		No.	%	No.	%	No.	%
Fever	81	25	30.86%	56	69.13%	81	81%
Cough with expectoration	46	19	41.3%	27	58.69%	46	46%
Appetite loss, weight loss	85	4	5.8	81	95.2%	85	85%
Tiredness	84	7	8.4	77	91.6%	84	84%
Head ache	36	25	69.44	11	30.56%	36	36%
Oral ulcer	35	13	37.2%	22	62.8%	35	35%
Painful swallowing	26	18	69.2%	8	30.8%	26	26%
Skin lesion	26	4	15.4	22	84.6%	26	26%
Loose stools	16	5	31.25%	11	68.75%	16	16%
Genital ulcer	15	6	40%	9	60%	15	15%

Associated clinical symptoms in HIV positive patients are shown in the [Table - 7]. Appetite loss, weight loss [85%] and tiredness [84%] were the commonest presenting symptoms followed by fever[81%], cough with expectoration[46%], head ache[36%], oral ulcer[35%], painful swallowing[26%], skin lesion[26%], loose stools[16%] and genital ulcer[15%].

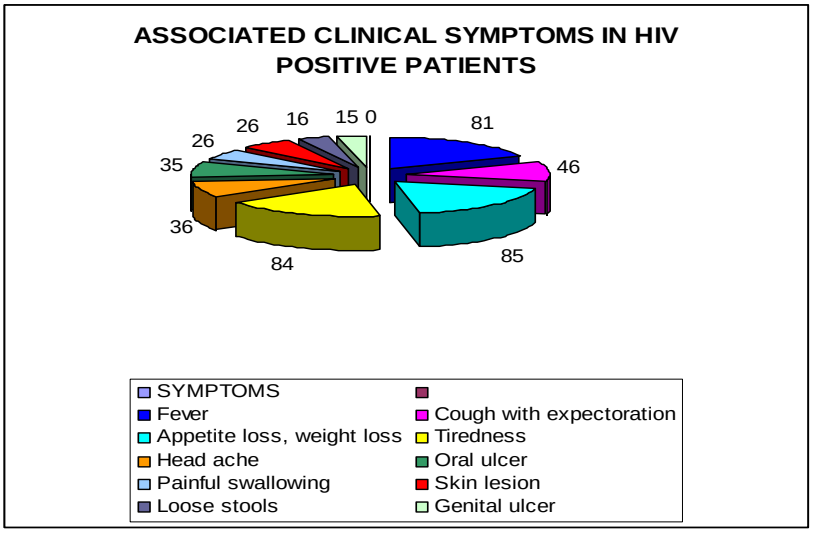


TABLE – 8

ASSOCIATED CLINICAL SIGNS IN HIV POSITIVE PATIENTS

Signs	No of cases	%
Wasting	91	91%
Fever	82	82%
Pallor	81	81%
Oral candidiasis	67	67%
Glossitis	52	52%
Black Nails	36	36%
Lymphadenopathy	32	32%
Oral hairy leukoplakia	17	17%
Genital lesion	16	16%
Seborrhoeic Dermatitis	4	4%
Herpes zoster	1	1%
Chronic Pruritic papular dermatitis	14	14%
Dyspnoea	27	27%
Pedal edema	21	21%
Retinopathy	3	3%

Associated clinical signs in HIV positive patients are shown in the [Table - 8]. Examination revealed that the patients had multi system involvement. 91% of patients had developed AIDS related cachexia also known as ‘wasting syndrome’. 82% of cases had fever , 70% were anaemic, 67% had oral candidiasis, 52% had Glossitis, nails of 36% of the cases showed black discolouration[black nails], 36% had lymphadenopathy, 17% had oral hairy leukoplakia, 16% had genital lesion, 14% had chronic pruritic papular dermatitis, 4% had Seborrhoeic dermatitis, 3% had retinopathy and 1% had herpes zoster.

Herpes zoster

oral candidiasis

Oral hairy leukoplakia

Seborrhoeic Dermatitis

Cold abscess

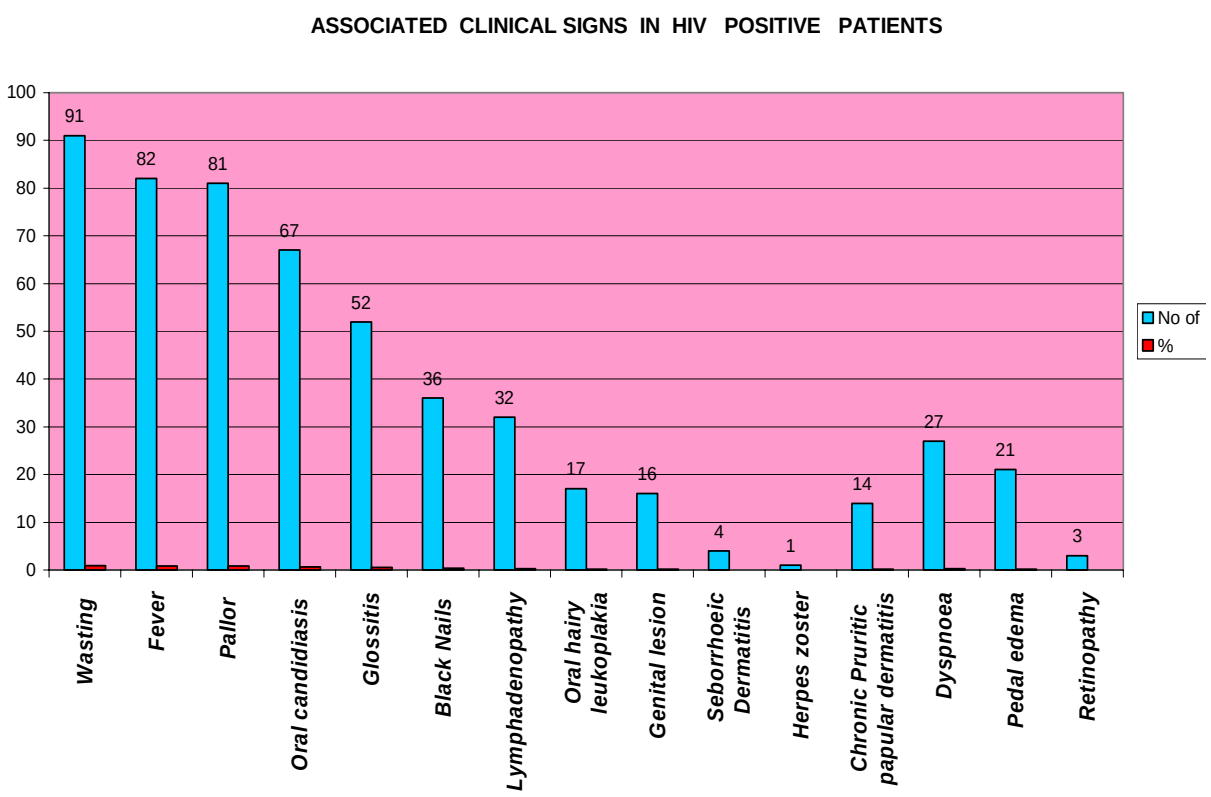


TABLE – 9

LYMPHADENOPATHY

Lymphadenopathy	No of cases	%
Cervical	21	21%
Cervical, Axillary	8	8%
Generalized	3	3%
Abdominal Lymphadenopathy	16	16%

Table 9 show that cervical lymphadenopathy was present in 21% of cases, 8% presented with cervical and axillary node enlargement, 3% had generalized lymphadenopathy and 16% had abdominal lymphadenopathy [ultra sonogram abdomen].

TABLE –10

GENITAL LESION

Genital Lesion	Male n=80		Female n=20		Total n=100	
	No.	%	No.	%	No.	%
Genital Herpes	8	10%	6	30%	14	14%
Wart	–	–	1	5%	1	1%
Cervical Carcinoma	–	–	1	5%	1	1%

Table 10 shows that 10% of male cases and 30% of female cases had genital herpes. Of the female cases 5% had genital wart and another 5% had cervical carcinoma.

TABLE – 11

CLINICAL FINDINGS ON EXAMINATION OF THE ABDOMEN

	No. of cases	%
Doughy Abdomen	7	7%
Hepatomegaly	33	33%
Splenomegaly	10	10%
Hepatosplenomegaly	2	2%
Ascites	5	5%

Clinical finding on examination of the abdomen is shown in the Table 11. 7% had doughy abdomen 33% of the cases had hepatomegaly, 10% had splenomegaly, and 2% had hepatosplenomegaly.

INVESTIGATIONS

TABLE – 12

Urine Culture Organism growth	No of cases	%
Escherichia coli	4	4%
Proteus	2	2%
Klebsiella pneumonia	1	1%

Urine culture report is shown in Table 12.

4% showed growth of Escherichia coli, 2% Proteus and 1% Klebsiella pneumonia.

TABLE – 13

Anaemia

Table 13 shows 70% of cases were moderately anaemic and 24% were severely anaemic.

Hemoglobin gm %	No of cases	%
<7	24	24%
7.1 – 10.9	70	70%
> 11	6	6%

TABLE 14

SPUTUM AFB **POSITIVE**

Table 14 shows sputum smear for AFB was positive in 16% of the cases.

No of cases **16**

TABLE 15

SPUTUM CULTURE

	No of cases	%
Proteus	2	2
Klebsiella Pneumonia	6	6
Aspergillus niger	1	1
Aceneto bacter	1	1
E.coli	2	2

Table 15 shows sputum culture report. 6% of the cases showed the growth of Klebsiella pneumonia, 2% showed E.coli, 2% showed Proteus, 1% Aspergillus niger and 1% Aceneto bacter.

TABLE – 16

X – RAY CHEST

	No of cases	%
Pleural effusion	14	14%
Consolidation	10	10%
Upper lobe fibrosis	2	2

X-ray features of the cases are shown in the Table 16.

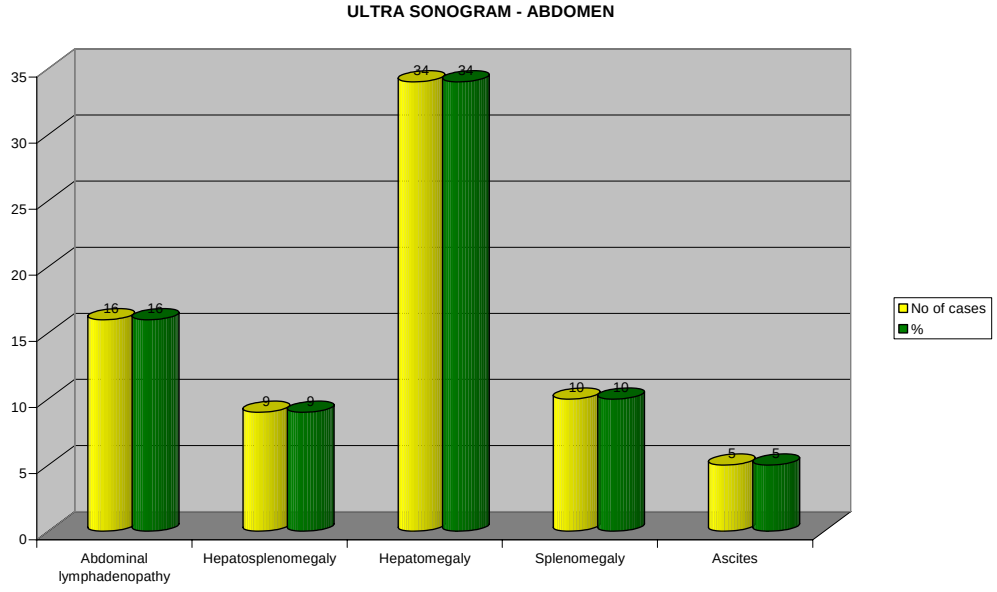
14% showed pleural effusion, 10% showed consolidation and 2% showed upper lobe fibrosis.

TABLE – 17

USG - ABDOMEN

	No of cases	%
Abdominal lymphadenopathy	16	16
Hepatosplenomegaly	9	9
Hepatomegaly	34	34
Splenomegaly	10	10
Ascites	5	5

Findings of ultra sonogram abdomen of the cases are shown in the Table 17. Abdominal lymphadenopathy was found in 16% of the cases, hepatomegaly in 34%, splenomegaly in 10%, hepatosplenomegaly in 9% and ascites in 5%.



Associated clinical conditions in HIV positive patients are shown in Tables 18, 19, 20 and 21.

TABLE – 18

ASSOCIATED CLINICAL CONDITIONS IN HIV POSITIVE PATIENTS

Respiratory system	**n=42**		**N=100**	
	No.	**%**	**No.**	**%**
Sputum AFB Positive Pulmonary tuberculosis	16	38.0%	16	16%
Klebsiella pneumonia	6	14.28%	6	6%
Tuberculous Pleural effusion	14	33.33%	14	14%
Other bacterial infections	6	14.28%	6	6%
TOTAL	42	100%	42	42%

Respiratory system disorder is shown in the Table 18.

Among the 100 cases 42% had respiratory illness.

38% of the respiratory illness was sputum smear positive tuberculosis, 33% was tuberculous pleural effusion and 28.5% were other bacterial infections.

TABLE – 19

GASTROINTESTINAL SYSTEM

	No of cases	%
Oral Candidiasis	67	67%
Esophageal Candidiasis	26	26%
Oral hairy leukoplakia	17	17%
Abdominal Tuberculosis	8	8%
Gastroenteritis	17	17%
Hepatitis – B. Infection	1	1%

Table 19 shows the gastrointestinal manifestations in the study group. 67% had oral Candidiasis, 26% had esophageal candidiasis, 17% had gastroenteritis, 17% had oral hairy leukoplakia, 8% had abdominal tuberculosis and 1% had acute Hepatitis B virus infection.

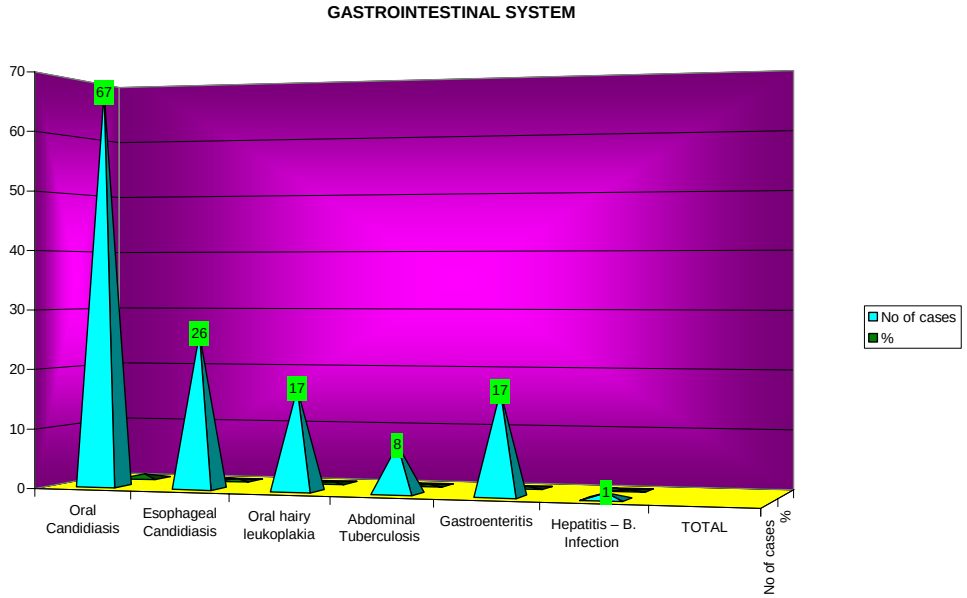


TABLE – 20

CENTRAL NERVOUS SYSTEM

	No of cases	n=33	n=100	
		%	No.	%
Cryptococcal Meningitis	15	45.45%	15	15%
Tuberculous Meningitis	6	18.18%	6	6%
Candidial Meningitis	2	6%	2	2%
HIV encephalitis	2	6%	2	2%
Tuberculoma	2	6%	2	2%
Toxoplasmosis	1	3%	1	1%
CMV retinitis	1	3%	1	1%
HIV retinopathy	2	6%	2	2%
Neurocysticercosis	1	3%	1	1%
Brain Abscess	1	3%	1	1%
TOTAL	33	100%	33	33%

Table 20 shows the Central Nervous System manifestations in the study group.

Of the 100 cases 33 presented with Central Nervous System manifestations. Among them 45.45% was Cryptococcal meningitis, 18.18% was tuberculous meningitis, 6% was Candidial meningitis, 6% was HIV encephalitis, 6% was Tuberculoma and 6% was found to have HIV retinopathy.Others including CMV retinitis, Toxoplasmosis, Neurocysticercosis and Brain Abscess -3% each were also found.

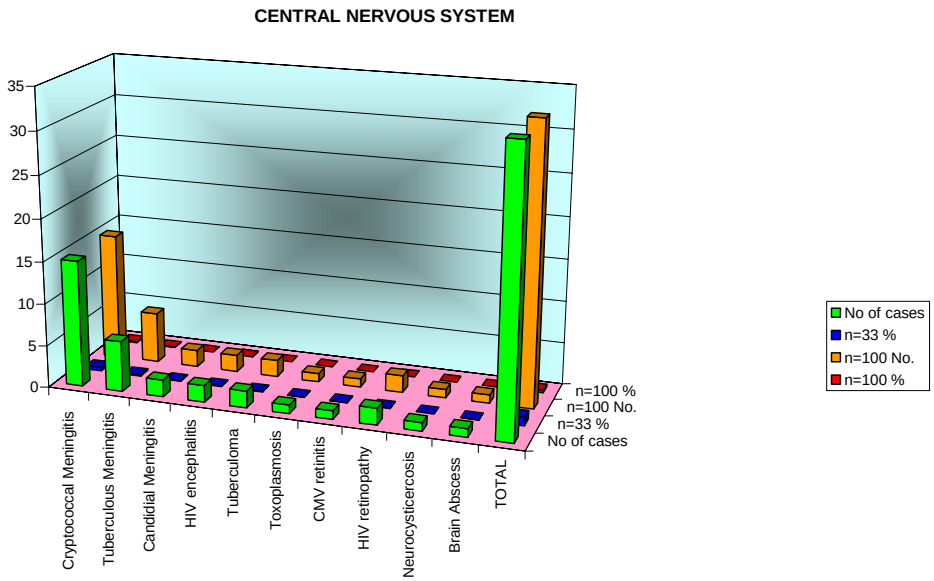

CENTRAL NERVOUS SYSTEM
35
30
25
20
15
10
5
0
Cryptococcal Meningitis
Tuberculous Meningitis
Candidial Meningitis
HIV encephalitis
Tuberculoma
Toxoplasmosis
CMV retinitis
HIV retinopathy
Neurocysticercosis
Brain Abscess
TOTAL
n=100 %
n=100 No.
n=33 %
No of cases
No of cases
n=33 %
n=100 No.
n=100 %

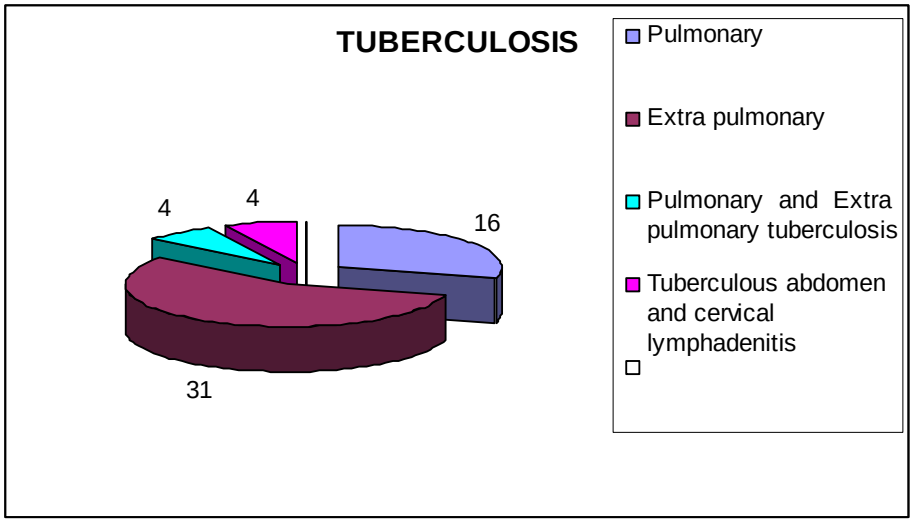
TABLE – 21

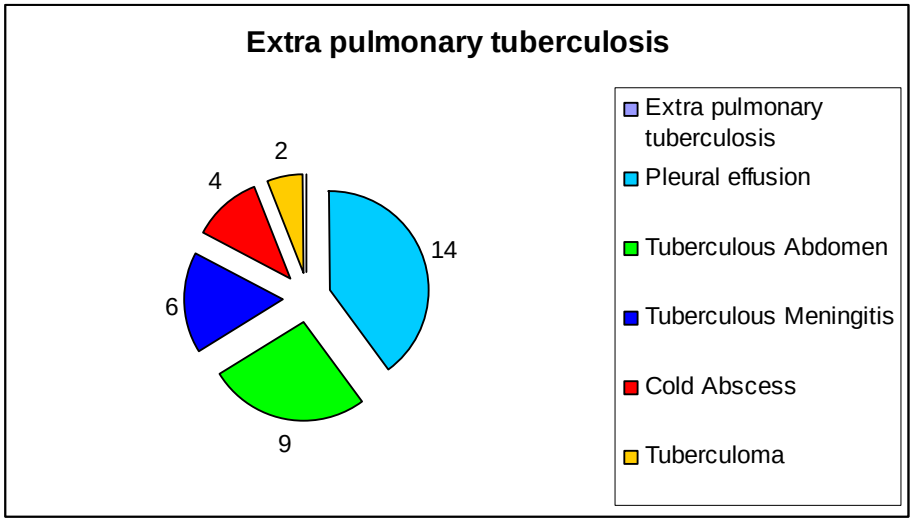
TUBERCULOSIS

	No. of cases	n=47 %	n=100 %
Pulmonary	16	34.04%	16%
Extra pulmonary	31	65.95%	31%
TOTAL	47	47%	47%
Pulmonary and Extra pulmonary tuberculosis	4	8.51%	4%
Tuberculous abdomen and cervical lymphadenitis	4	8.51%	4%
Extra pulmonary tuberculosis			
Pleural effusion	14	29.78%	14%
Tuberculous Abdomen	9	17.02%	9%
Tuberculous Meningitis	6	12.76%	6%
Cold Abscess	4	8.51%	4%
Tuberculoma	2	4.25%	2%

Various presentation of tuberculosis is shown in Table 21.

Of the 100 cases 47 cases presented with tuberculosis. Among them 65.9% had extra pulmonary and 34% had pulmonary tuberculosis. 8.5% had both pulmonary and extra pulmonary tuberculosis and another 8.5% had tuberculosis of abdomen and cervical lymphadenitis. Among extra pulmonary tuberculosis 29.7% was Pleural effusion, 17% was Tuberculous Abdomen, 12.76% was Tuberculous Meningitis, 8.5% was cold Abscess and 4.25% was Tuberculoma.


TUBERCULOSIS
4
4
16
31
Pulmonary
Extra pulmonary
Pulmonary and Extra pulmonary tuberculosis
Tuberculous abdomen and cervical lymphadenitis


Extra pulmonary tuberculosis
2
4
14
6
9
Extra pulmonary tuberculosis
Pleural effusion
Tuberculous Abdomen
Tuberculous Meningitis
Cold Abscess
Tuberculoma

DISCUSSION

DISCUSSION

Although the Human Immunodeficiency Viruses are the initial causative agents in AIDS, most of the morbidity and mortality seen in the case of AIDS patient results from the opportunistic infections which take advantage of the lowered cellular and humoral defences of the patient. A wide variety of these infections are encountered in the AIDS population, including bacteria, fungi, viruses and protozoa. Very often, these represent not new infections but the reactivation of old infection.[72]

In the present study out of 100 HIV positive patients 80% were males and 20% were females. This is similar to NACO findings [70]: Strong association between HIV positivity and sex is found that males are more affected.

The age ranged between 13 to 60 in males and 19 to 53 in females. The maximum number of patients was in the 30-39 years age group followed by 40-49 years. 81.25% of males and 85% of females were in sexually active and economically productive group of 15 to 44 years. This population yet not done adequately for their family and is going to leave orphans and widows who are HIV positive.

Poor literacy status is associated with high rate of infection [71]

probably because of low awareness levels about risk factors among them the low self estimate may provoke them taking more risk.

The commonest mode of transmission (99%) was due to sexual contact. Most of the males were married and 57% had history of extra marital sexual contact and 51% had premarital contact. 20% of the males were unmarried. One case had acquired HIV infection from his infected parents who died of AIDS.

In males the commonest occupation was driver [21.25%], followed by laborer in various fields [40%].

The HIV infection in females revealed a sorry story in our population. Most of the females were homemakers and 20% were labourers. Two persons gave history of extra marital sexual contact. Women are at the mercy of their counterparts and are silent sufferers, they do not have the right to ask for contraception and suffer a deadly disease just because of their partners.

50% of the cases came to know about their HIV positivity status only after hospitalization.

All the patients presented with more than one symptom. Appetite loss [85%] and tiredness [84%] were the commonest presenting symptoms followed by weight loss of more than 10% (85%). Fever of more than 1 month duration was found in nearly 69.13% of these patients, while cough (46%), head ache [36%], skin

lesions [26%] and diarrhoea (16%) were the other common manifestations seen among the patients studied. (32%) patients presented with lymphadenopathy. Cervical lymph nodes were the commonest lymph nodes found to be enlarged and were seen in 21% of the patients. These observations are similar to those in the study published in 124 Journal, Indian Academy of Clinical Medicine _ Vol. 4, No. 2 _ April-June 2003.

81% of the cases were anaemic.

Oral candidiasis was the most common (67%) opportunistic infection and our finding is similar to the report of NACO[73] and T K Giri et al. [73] But Kaur et a1[74] from Vellore have reported oral candidiasis as the second most common infection in AIDS patients. Ayyagari et a1[75] have reported very low incidence of candidiasis (27.7%).

26 patients had symptom of dysphagia and were found to be having oral and esophageal candidiasis. Presence of oral candidiasis and weight loss is the marker of HIV disease progression. Hence regular examination of oral cavity is important.

Oral hairy leukoplakia *(OHL)*: Worldwide, prevalence of OHL among HIV infected individual ranges from 0 to 26 per cent 54. One study in south India reported OHL in 4 per cent of 594 HIV positive individuals 4. In our study 17% of cases had OHL.

Tuberculosis [TB] is endemic in India and is the common cause of death in AIDS patients. Its prevalence is reported to be increasing in patients with HIV infection.

Mycobacterium tuberculosis was the commonest isolate reported in few studies from India. [74], [75], [76]. But we observed it as the second most common pathogen (47%) as NACO.[72] Pulmonary tuberculosis was observed in 16% and extra pulmonary tuberculosis in 31% of cases. HIV infection is a strong risk factor for the active tuberculosis in persons with latent M. tuberculosis infection. The risk of active tuberculosis in HIV seropositive persons is 14% over 2 years - contrasting strikingly with the estimated 10% lifetime risk in H IV negative persons with latent tuberculosis infection.

Abdominal tuberculosis, a frequently recognized form of extra pulmonary tuberculosis is increasing with increasing incidence of HIV infection, as said in The API Medicine Update volume 17, 2007. In our study 9% had abdominal tuberculosis. All cases had doughy abdomen on examination and ultra sonogram abdomen showed enlargement of mesenteric, peri-pancreatic, peri-portal and para-aortic group of lymph nodes. These nodes were seen as conglomerulate mass and / or as scattered enlarged lymph nodes with hypo echoic center because of necrosis.

Despite the prevalence of pulmonary and extra pulmonary TB in Indian patients, TB meningitis is less common than cryptococcal meningitis. In our study 6% of cases had tuberculous meningitis.

The key therapeutic principles underlying the treatment of HIV-TB are:

1. The treatment of TB should precede the treatment of HIV infection, i.e. HAART.
2. Patients already on HAART should continue the same treatment with appropriate modifications, in HAART and ATT.
3. Patients who are not receiving HAART, the need and the time of initiation of HAART have to be decided on individual basis after assessing the CD4 count and type of TB.

Treatment guidelines for HIV-infected patients are identical to the standard regimens recommended for those without HIV with two exceptions. Directly observed therapy [DOT] is the standard of care. DOTS should be initiated with isoniazid, rifampicin, ethambutol and pyrazinamide [HREZ] for first two months followed by isoniazid and rifampicin for subsequent 7 months. First exception is that treatment regimen should be daily or thrice a week during the continuation

phase. Second is that continuation phase should be extended to seven months. All therapeutic combinations should include a rifamycin (rifampicin or rifabutin) and patients should be monitored for drug interactions with protease inhibitors. Patients with risk factors for drug-resistant *M tuberculosis* infection may need treatment with three or more drugs.

Herpes zoster can occur early in the course of HIV disease and generally precedes other skin manifestations of HIV disease. In patients with

HIV, it can present with necrotizing ulcers in a multidermatomal pattern, can last longer than the usual 2-3 wk, and heal leaving prominent scars. There was no associated increase in mortality

1% in our study group showed Herpes zoster infection, the incidence is low probably since it occurs in early stage of the disease and most of our patient presented with stage III or IV.

Papular pruritic eruption (PPE) is a unique dermatosis associated with advanced HIV infection, characterized by sterile papules, nodules or pustules with a hyperpigmented, urticarial appearance and pruritis. In our study 14% of cases were found to have chronic papular pruritic eruption.

Kaposi's sarcoma was not found in our study.

Most HIV infected persons are also infected with HSV-1 and HSV-2. Primary infection with HSV, at either the oral or genital sites, is often characterized by multiple lesions. In our study 10% of males 30% of females had genital herpes. Genital herpes (14%) was the commonest genital lesion observed among the study participants followed by genital warts (1%).

This has similar incidence as in the study conducted by J Chakravarty, H Mehta –‘ Study on Clinico-epidemiological Profile of HIV Patients in Eastern India’ published in JAPI • VOL. 54 • NOVEMBER 2006.

Several studies have found an increased prevalence of cervical dysplasia, a precursor lesion for cervical cancer, among HIV-infected women (78). Several studies have documented that a higher prevalence of cervical dysplasia among HIV-infected women is associated with greater immunosuppression. In addition, HIV infection may adversely affect the clinical course and treatment of cervical dysplasia and cancer (79). In our study 1% had stage II cervical carcinoma.

Cryptococcal meningitis is an opportunistic infection by the yeast C.neoformans and is the presenting manifestation of AIDS in about a third of these patients. It is the fourth most commonly recognized cause of life threatening infection among these patients.

Infection of the brain and meninges is the most common clinical manifestation of cryptococcosis and the most common cause of death from that disease.

The incidence of Cryptococcal meningitis varies from place to place. The incidence of Cryptococcal meningitis among HIV cases in our study is 15% which is comparable to other reports (Ayyagiri *et al* [80] 5.6%, Bogaerts et al 3 19%, Rakhmanova *et al* [81] 17%, Silva Rosa *et al* 45.8%).

Thus, the incidence of Cryptococcal meningitis has been found to be very high in our region and was the most common opportunistic pathogen isolated from CSF among all the pathogens put together.

The most common ophthalmic opportunistic infection in India is CMV retinitis, which almost always occurs in patients with CD4 counts <50 Cells/L.

The second most common ophthalmic manifestation of HIV infection is non-infectious retinopathy (HIV retinopathy), reported in 13-15 per cent of HIV patients presenting to an ophthalmologist. This condition, characterized by cotton wool spots, can be an early sign of HIV infection, and must be differentiated from diabetic and hypertensive retinopathy. In our study CMV retinitis was 1% and HIV retinopathy was 2%.

Toxoplasmic encephalitis (TE) is caused by the protozoan Toxoplasma gondii. Disease occurs almost exclusively because of reactivation of latent tissue cysts. In our study one case had Toxoplasma encephalitis.

One among the study participants had Neurocysticercosis.

Strictly speaking, wasting syndrome is not an opportunistic infection. In our study 91% of cases had wasting syndrome.

Wasting in AIDS is now thought to be, in part, a catabolic process that preferentially degrades muscle mass (82). Thus, in addition to previously available therapies designed to boost appetite and caloric intake (e.g. dronabinol and megestrol acetate), anabolic steroids such as oxandrolone, testosterone replacement, and recombinant human growth hormone (83 are now given in an attempt to reverse this chronic breakdown state. Together with more aggressive antiretroviral regimens and an increased understanding of the nutritional requirements of patients with advanced AIDS (84), these new drugs have improved the ability to halt and reverse the previously inexorable loss of lean body mass.

In our study, only 1 patient was positive for HbsAg, which is in contrast to Western data quoting 90- 95% incidence [85]; this is probably because of the fact that most of the infections take

place via heterosexual contact and not through infected needles and blood transfusion.

Oral hairy leukoplakia *(OHL)*: Worldwide, prevalence of OHL among HIV infected individual ranges from 0 to 26 percent [86]. One study in south India reported OHL in 4 per cent of 594 HIV positive individuals[87]. In our study 17% of cases had OHL.

HIV infection and psychiatric disorders have a complex relationship. Being HIV infected could result in psychiatric disorders as a psychological consequence of the infection or because of the effect of the HIV virus on the brain. In our study one case presented as schizophrenia which probably be a primary psychiatric illness and another as pseudo dementia.

BLACK NAILS:

Black discolouration of the nails was found in 36% of the cases. It is the new clinical finding noted in the study group. It is said that black discolouration of the nails aiso occurs as a side effect of anti-retro viral therapy, but those who wer on anti-retro viral therapy were not included in our study.

OTHER OBSERVATIONS

Hyper pigmentation of the tongue, skin or palms was noted in 13% of cases.

Most cases were noted to be having normochromic normocytic anaemia and Liver function test showed reversal of albumin globulin ratio. Most of the cases, 91% presented with features of III or IV stage of the disease and were seriously ill.

Black nails

CONCLUSION

CONCLUSION

The most common age group infected was in the range of 30 -39 years.

Most of the cases were aware of their HIV positivity status only after admission in the hospital for their illness.

Heterosexual contact was the commonest mode of transmission.

Patients presented with more than one symptom, the common being fatigue, loss of weight, loss of appetite, fever and chronic cough.

Patient had multisystem involvement. 91% of patients had developed AIDS related cachexia also known as 'wasting syndrome'.

Oral candidiasis was the commonest opportunistic infection followed by tuberculosis.

Presence of oral candidiasis and weight loss can be considered as a marker of HIV disease progression.

Most common genital lesion was due to Herpes simplex virus.

Common haematological abnormality observed was anaemia.

The incidence of Cryptococcal meningitis has been found to be very high in our region and Cryptococcus neoformans was the most common opportunistic pathoge[74] ated from CSF among all the pathogens put together.

Cryptococcal infection should be suspected in all cases of meningitis among HIV infected persons. It most commonly develops over several weeks with insidious onset of headache, malaise, and fever. Early diagnosis and treatment may alter the prognosis for these patients.

Extra pulmonary tuberculosis was more common than pulmonary tuberculosis whereas tuberculous meningitis was less frequent than cryptococcal meningitis.

Only one case was Hepatitis B antigen positive.

Chronic Papular pruritic eruption (PPE) was found in many cases Kaposi's sarcoma was not found in our study.

Black discolouration of the nails was the new clinical finding in the study group.

Early diagnosis of opportunistic infection and prompt treatment not only helps HIV-positive people to live longer, healthier lives, delaying the progression towards AIDS but also prevent TB and other transmissible opportunistic infections from spreading to others.

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APPENDIX

PROFORMA

COIMBATORE MEDICAL COLLEGE & HOSPITAL
A STUDY OF 100 CASES OF HIV

MEDICAL UNIT **V**

Name of the patient: Gender: M/F

Age : I.P.No.:

Name of the spouse: STD No.:

Marital of the patient: Date of admission:

Single/Married/Separated/Widow/Widower

Address : Spouse reactive for HIV I&II

Yes/No

Occupation: Education:

Income:

When the patient knows that he/she is HIV positive:

Complaints :

H/o present illness:

Symptoms	Duration	Symptoms	Duration	Symptoms	Duration
Fever		Head ache		Oral ulcer	
Cough		Appetite loss		Painful swallowing	
Sputum		Weight loss		Skin lesion	
Breathlessness		Tiredness		Loose stools	
Chest pain		Nausea/vomiting		Genital ulcer	
hemoptysis		Visual disturbance		Anal ulcer	

Other illness

H/O Past illness:

Risk factor for acquiring infection: Sexual –PMC/EMC/Marital

IVDrug abuse/blood transfusion/needle prick/vertical transmission.

Family history:

Clinical features:

Fever	Wasting
Pallor	Pulse rate
Dyspnoeic	BP
Cyanosis	Weight in Kg
Icterus	Black nail
Clubbing	Pedal edema

Skin-Seborrhoeic dermatitis/mucocutaneous herpes simplex /herpes zoster/ Kaposis sarcoma/molluscum contagiosum/scabies/fungal skin infection

Mouth - Oral candidiasis/ Oral leukoplakia/ Glossitis/chelitis

Lymphadenopathy:

Ano genital : Rash/ condyloma/ mucocutaneous herpes simplex/STD

Cardiovascular System:

Respiratory System:

Abdomen :

Central Nervous System:

INVESTIGATIONS

Urine -albumin

Sugar

Deposit

Urine Culture

Motion ova/cyst

Motion C/S

Complete Hemogram:

Hbgm%

TC cells/mm³

Dc

ESR mm/hr

Platelets cells/mm³

Pathologist opinion

Peripheral smear for MP/MF

Blood sugar

Blood Urea

Sr. creatinine

Sr. electrolytes

Na+ meq/L

K+ meq/L

LFT

SGOT IU/L

SGPT IU/L

ELISA for HIV I & II

VDRL

Blood culture

Sputum for AFB staining

Sputum culture

Sputum for fungal culture

HbsAg

HCV Ab

Blood Widal

USG abdomen

CT

CSF analysis

Pleural Fluid Analysis

SAP IU/L

Sr. Bilirubin mg%

Sr. proteins Total gm%

Albumin gm% CD4 Cell count

Globulin gm%

ECG:

X-ray chest:

ABBREVIATIONS used in master chart

M-Male
F- Female
m- Married
unm-unmarried
S-Separated
W-widow
R-Reactive
NR-Non reactive
NK-not known
L-Labourer
DA-Diploma Agri
y-Years
Mn-Month
d-Day
Visual disturbance- blurring of vision, double vision
CNS symptoms- disorientation, fits, difficulty in using limbs
Seborrhoeic dermatitis
KS-Kaposi's sarcoma
OC-Oral candidiasis
CPPD-Chronic pruritic papular dermatitis
OLP- Oral hairy leukoplakia
B/L C- B/L Cervical lymphadenopathy
B/L C, A- B/L Cervical, Axillary lymphadenopathy
Cold A- Cold abscess
Retina- P-Papilloedema, CMVR- CMV retinopathy, HIVR- HIV retinitis
N-Normal
CVS-Cardiovascular system
RS-Respiratory system- B-Right pleural effusion
C-B/L pleural effusion
D-Right lower lobe consolidation
E-Right upper lobe consolidation
F-Left upper lobe fibrosis
G-Left lower lobe consolidation
H- Right upper lobe fibrosis
I- Left pleural effusion
J-Right pyothorax
K-B/L Wheeze, crepts
Abdomen- O-Doughy, O,1-Doughy, Para aortic node felt
Oa-mutiple para aortic nodes
O,2- Doughy, right iliac fossa mass
4- Hepatosplenomegaly
4a-hepatomegaly
4b-splenomegaly
4c- multiple enlarged lymph nodes-
portahepatis, coeliac, paraaortic both iliac
suggestive of tuberculosis of abdomen
4d- grade 1 fatty liver
4e- ascending colon thickening

3-Ascites,
Cx- endocervix irregularly thickened-12mm uterus bulky

CNS-Central nervous system
5- Right upper motor neuron facial palsy, right upper limb weakness
6-Neck stiffness
7-Right sided weakness
8-GTCS
9- Pseudo-dementia, patchy memory lapses
10- Left hemi paresis
11- Schizophrenia
12- Proximal muscle weakness, muscle wasting
13-Neck stiffness, cranial nerve palsy , right hemiparesis
Urine culture: a- proteus group grown
b- Escherichia coli grown culture
c- Klebsiella pneumonia grown culture
NFG- Normal flora grown
Pathologist opinion- d- Dimorphic anaemia
e- microcytic hypo chromic anaemia
f- marked neutrophilic leucocytosis
g- normocytic to microcytic anaemia
h- normochromic normocytic anaemia
r- Relative neutrphilia
Blood WIDAL –j- O&H +1 in 100 dilution
X-RAY chest- Q- thick walled cavity left mid zone
T- B/T Pulmonary tuberculosis
U- upper mediastinal Widening
ECG- ST-sinus tachycardia
CSF- NO- No bacteria
Urine culture
Ac- acinetobacter grown

S.p- S.pyogenes
K.p- Klebsiella pneumonia
c.neg.S.- coagulase negative Staphlococcus
Str.- Streptococcus
E.c-E coli
Pr- Proteus group grown
Asp- Aspergillus niger grown
Ps.- Pseudomonas
C.a - Candida

CT-brain
c1-multiple abscess in brain
c2- infarct in left parieto occipital cortex
c3- chronic SDH
c4- right frontal, parietal region ring enhancing multiple lesion

c5- ring enhancing lesion with perilesional edema in right parietal region
c6- atrophic change
c7- left frontal ring enhancing lesion with perilesional edema
c8- gliosis

CSF analysis

c9- 0 to 15 yeast cells
Lc- lymphocytes
ce- cells
s- sugar
p- protein
g- globulin
cl- chloride

Pleural fluid analysis

P1- 2000pus cells, S.pyogenes grown, protein4.8, albumin1.9
LDH- Lactate dehydrogenase